

Claims

1           1.       A method for identifying phenotypes that vary in cell lines as a result of  
2       genetic variation, comprising:

3           (a)       measuring one or more phenotypes in cell lines from one or more pedigrees;  
4       and

5           (b)       testing whether the pattern of phenotype data in the cell lines conforms to the  
6       rules of Mendelian transmission,

7           wherein conformation of said phenotype data to the rules of Mendelian transmission  
8       is indicative that said phenotype varies in cell lines as a result of genetic variation.

1           2.       A method for identifying phenotypes that vary in cell lines as a result of  
2       genetic variation, comprising:

3           (a)       measuring one or more phenotypes in cell lines from one or more pedigrees;  
4       and

5           (b)       testing whether the pattern of phenotype variation in the cell lines segregates  
6       in the pedigree so as to produce a LOD score of at least 2 with one or more loci, and wherein  
7       detection of a LOD score of at least 2 is indicative that said phenotype varies in cell lines as a  
8       result of genetic variation.

1           3.       The method of claim 1, wherein the phenotype is the mRNA level of a  
2       selected gene.

1           4.       The method of claim 2 where the LOD score is at least 3.

1           5.       The method of any of claims 1 or 2, wherein the cell lines are derived from  
2       the CEPH pedigrees.

1           6.       The method of any of claims 1 or 2, wherein the gene or genes responsible for  
2       the inter-cell line variation in phenotype are mapped to chromosomal loci by comparison of  
3       the pattern of segregation of the phenotype in the cell lines with the pattern of segregation of  
4       known mapped variances in the same cell lines.

1           7.       The method of claim 4, wherein one or more candidate genes are evaluated by  
2 determining if their chromosomal position is one of the chromosomal positions (loci) that  
3 displays segregation with the phenotype.

1           8.       The method of any of claims 1 or 2, wherein at least 15 cell lines from related  
2 individuals are tested.

1           9.       The method of any of claims 1 or 2, wherein the cells are subjected to a  
2 treatment before measuring the phenotype, the treatment selected from the group consisting  
3 of:

- 4           a. addition of a compound to the cells,  
5           b. change in the nutritional environment of the cells, and  
6           c. change in the physical environment of the cells.

1           10.      A method for identifying mRNAs that vary in levels as a result of genetic  
2 variation, comprising:

- 3           a. measuring levels of one or more specific mRNAs in cell lines from one or more  
4 pedigrees; and  
5           b. testing whether the mRNA levels of said one or more specific mRNAs in said cell  
6 lines conforms to the rules of Mendelian transmission,  
7           wherein conformation of any of said mRNA levels to the rules of Mendelian  
8 transmission is indicative that said mRNA level varies in cell lines as a result of genetic  
9 variation.

1           11.      The method of claim 10, wherein said cell lines are derived from one or more  
2 of the CEPH pedigrees.

1           12.      The method of claim 10, wherein the gene or genes responsible for the  
2 intersubject variation in levels of specific mRNAs are mapped to chromosomal loci by  
3 comparison of the pattern of segregation of the mRNA levels in the cell lines with the pattern  
4 of segregation of variances that are already mapped to the human genome.

1           13.     The method of claim 10, wherein at least 100 cell lines from related  
2 individuals are tested.

1           14.     The method of claim 10, wherein said cells are subjected to a treatment before  
2 performing the RNA analysis, the treatment selected from the group consisting of:

- 3           a. addition of a compound to the cells,  
4           b. change in the nutritional environment of the cells, and  
5           c. change in the physical environment of the cells.

1           15.     A method for the identification of phenotypes that vary among cell lines as a  
2 consequence of genetic variation, the method comprising:

- 3           a. Determining the genotype of a set of cell lines from unrelated subjects at candidate  
4 genes for the phenotypes of interest;  
5           b. measuring the phenotype in the cell lines; and  
6           c. Measuring whether genetic variation among the cell lines correlates with variation  
7 in the phenotype.

1           16.     The method of claim 15 where at lest 20 cell lines are analyzed.